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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,213	02/14/2002	Chung-Hsiun Wu	13062-002001	3100

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/077,213	WU ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *30 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *7 and 13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12 and 17-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the restriction/election requirement received on 4/16/04 has been entered. Applicant's election without traverse of the species "antibody" is acknowledged. Claims 1-32 are pending in the instant application. Of these, claims 7 and 13-16 have been withdrawn as being drawn to subject matter non-elected without traverse. Claims 1-6, 8-12, and 17-32 are currently under examination in the instant application. An action on the merits follows.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 3-6, 8, 17, 19–20, 23-26, 29, and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,462,254 (10/8/02), hereafter referred to as Vernachio et al. The applicant claims methods of preparing a fusion protein comprising administering to a mammal a nucleic acid encoding a fusion protein which contains a first amino acid sequence and a second amino acid sequence, wherein the second amino acid sequence contains a first member of a specific binding pair, removing a biological sample from the mammal that contains the fusion protein, and isolating the fusion protein by binding second member of the specific binding pair to the fusion protein. The applicant further claims methods of isolating a target binding molecule which is an antibody by following the method of preparing a fusion protein and further contacting the fusion protein with a solution comprising the target antibody and isolating the antibody by means of its binding to the first member of the fusion protein. The applicant also claims said methods wherein the sample is serum or a tissue lysate, wherein the second member of the specific binding pair is a monoclonal antibody, wherein the first member of the specific binding pair is a peptide of at least 5 amino acids in length, and/or wherein the fusion protein is immobilized.

Vernachio et al. teaches methods of isolating and concentrating a fusion protein which comprises a capture tag and a detection tag comprising administering to a mammal a nucleic acid encoding a fusion protein comprising a capture tag sequence and a detection tag sequence and capturing the fusion protein from a sample from the mammal with an antibody that specifically binds to the capture tag sequence (Vernachio et al., columns 4, 7, and 13-14, see claims 1-15). The capture tag sequence is the "second amino acid sequence" of the fusion protein and the "first member of a specific binding pair", while the antibody which recognizes the capture tag is the

"second member of the specific binding pair". Vernachio et al. further teaches that the capture tag can be a peptide more than 5 amino acids long, see column 14, claim 3; and that the antibody can be a monoclonal antibody, see column 5, lines 51-56). Vernachio et al. also teaches the immobilization of the fusion protein to a solid surface such as a membrane, microtiter dish, or magnetic bead (Vernachio et al., column 6, lines 57-67). In addition, Vernachio et al. teaches that the sample from the mammal containing the fusion protein can be serum or a tissue lysate (Vernachio et al., column 11, lines 28-37, and column 12, lines 25-67). Finally, Vernachio et al. teaches that the purified fusion protein can be used in binding assays with antibodies which recognize and bind to detection tag sequence present in the fusion protein (Vernachio et al., columns 7-8 and 13-14, see in particular claim 4). Thus, by teaching all the elements of the claims as written, Vernachio et al. anticipates the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 10-11, 18, 21-22, 27-28, and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,462,254 (10/8/02), hereafter referred to as Vernachio et al., in view of U.S. Patent No. 5,726,044 (3/10/98), hereafter referred to as Lo et al. The applicant claims methods of preparing a fusion protein comprising administering to a mammal a nucleic acid encoding a fusion protein which contains a first amino acid sequence and a second amino acid sequence, wherein the second amino acid sequence contains a first member of a specific binding pair, removing a biological sample from the mammal that contains the fusion protein, and isolating the fusion protein by binding second member of the specific binding pair to the fusion protein. The applicant further claims methods of isolating a target binding molecule which is an antibody by following the method of preparing a fusion protein and further contacting the fusion protein with a solution comprising the target antibody and isolating the antibody by means of its binding to the first member of the fusion protein. In addition, the applicant claims said methods wherein the first member of the specific binding pair is an Fc domain of an immunoglobulin, and/or wherein the first amino acid sequence is cleaved from the second amino acid sequence.

Vernachio et al. teaches methods of isolating and concentrating a fusion protein which comprises a capture tag and a detection tag comprising administering to a mammal a nucleic acid

encoding a fusion protein comprising a capture tag sequence and a detection tag sequence and capturing the fusion protein from a sample from the mammal with an antibody that specifically binds to the capture tag sequence (Vernachio et al., columns 4, 7, and 13-14, see claims 1-15). The capture tag sequence is the "second amino acid sequence" of the fusion protein and the "first member of a specific binding pair", while the antibody which recognizes the capture tag is the "second member of the specific binding pair". Vernachio et al. further teaches that the capture tag can be a peptide more than 5 amino acids long, see column 14, claim 3; and that the antibody can be a monoclonal antibody, see column 5, lines 51-56). Vernachio et al. also teaches the immobilization of the fusion protein to a solid surface such as a membrane, microtiter dish, or magnetic bead (Vernachio et al., column 6, lines 57-67). In addition, Vernachio et al. teaches that the sample from the mammal containing the fusion protein can be serum or a tissue lysate (Vernachio et al., column 11, lines 28-37, and column 12, lines 25-67). Finally, Vernachio et al. teaches that the purified fusion protein can be used in binding assays with antibodies which recognize and bind to detection tag sequence present in the fusion protein (Vernachio et al., columns 7-8 and 13-14, see in particular claim 4).

Vernachio et al. differs from the instant invention by not teaching that the capture tag sequence is an Fc domain of an immunoglobulin. Vernachio et al. however teaches that the capture tag sequence is a sequence of amino acids that specifically binds to a ligand such as an antibody (Vernachio et al., column 2, lines 20-21, and column 2). Vernachio et al. further teaches that the particular capture tag sequence is not critical to the invention, and that the capture tag is chosen for its ability to concentrate the fusion protein (Vernachio et al., column 5, lines 11-16). Lo et al. provides motivation for using an Fc region of an immunoglobulin as a "capture tag

sequence" in the fusion protein provided by Vernachio. Lo et al. teaches nucleic acid vectors for expressing a fusion protein in mammalian cells wherein the fusion protein comprises an Fc region of an immunoglobulin linked by a protease cleavage site to a selected target polypeptide (Lo et al., columns 3-4). Lo et al. further teaches that the presence of the Fc region of an immunoglobulin in the fusion protein allows for increased production of the target protein and ease of collection because the secreted fusion protein can be collected without the need for cell lysis and can be purified using common reagents including antibodies and protein A (Lo et al., column 2, especially lines 29-35, and column 3, lines 9-23). Lo et al. further teaches the advantages of including the protease cleavage site in the fusion protein because the target polypeptide can be easily separated from the Fc region used to purify the fusion protein (Lo et al., columns 3 and 9). Note as well that Lo et al. teaches that protease inhibitors can also be administered to prevent cleavage of the fusion protein by proteases (Lo et al., column 16). Thus, based on the motivation to include the Fc region of an immunoglobulin and a protease cleavage site in a fusion protein in order to facilitate and improve the purification of the fusion protein as taught by Lo, and based on the teaching of Vernachio et al. that the "capture tag sequence" should be selected based on its ability to concentrate the protein, it would have been *prima facie* obvious to the skilled artisan at the time of filing to use the Fc region linked to a protease cleavage site as taught by Lo et al. as the "capture tag sequence" in the fusion proteins taught by Vernachio et al. Furthermore, in view of the successful use of the Fc region to purify fusion proteins as taught by Lo et al., and the high level of skill in the art of molecular biology at the time of filing, the skilled artisan would have had a reasonable expectation of success in

modifying the vectors encoding a fusion protein taught by Vernachio et al. to include the nucleic acid sequence encoding the Fc region and the protease cleavage site as taught by Lo et al.

Claims 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,462,254 (10/8/02), hereafter referred to as Vernachio et al., in view of U.S. Patent No. 5,726,044 (3/10/98), hereafter referred to as Lo et al. , as applied to claims 2, 10-11, 18, 21-22, 27-28, and 30-31 above, and further in view of US Patent No. 5,703,055 (12/30/97), hereafter referred to as Felgner et al. The applicant claims methods of isolating a target binding molecule which is an antibody comprising administering to a mammal a nucleic acid encoding a fusion protein which contains a first amino acid sequence and a second amino acid sequence, wherein the second amino acid sequence contains a first member of a specific binding pair, removing a biological sample from the mammal that contains the fusion protein, isolating the fusion protein by binding second member of the specific binding pair to the fusion protein, further contacting the fusion protein with a solution comprising the target antibody and isolating the antibody by means of its binding to the first member of the fusion protein. In addition, the applicant claims said methods wherein the first member of the specific binding pair is an Fc domain of an immunoglobulin, and wherein the target antibody is generated by immunizing an animal with a nucleic acid construct encoding the fusion protein.

The teachings of Vernachio et al. and Lo et al. as they apply to claims 2, 10-11, 18, 21-22, 27-28, and 30-31 are presented in detail above. While Vernachio et al. does teach administering the nucleic acid to the animal in order to produce the fusion protein through binding to the detection tag sequence, and further teaches that the target antibody capable of

binding the fusion protein can be made by challenging the animal with the detection tag, Vernachio et al. does not specifically teach that the nucleic acid encoding the fusion protein is used to challenge the animal to produce the target antibody (Vernachio et al., column 5, lines 53-56). Felgner et al. supplements Vernachio et al. by demonstrating that nucleic acid immunization with an antigenic polypeptide efficiently produces antibodies specific to the immunizing antigen (Felgner et al., columns 38-39 and 42). Thus, based on the teachings of Vernachio et al. that the target antibody can be made by challenging an animal with the fusion protein, and the teachings of Felgner et al. that nucleic acid immunization with an antigen efficiently produces antigen-specific antibodies, it would have been *prima facie* obvious to the skilled artisan to prepare the target antibodies by immunizing an animal with the nucleic acid encoding the fusion protein as taught by Vernachio et al. or Vernachio et al. in view of Lo et al. with a reasonable expectation of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-18 and 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 17-18, and 29-31 are dependent claims that depend on claims 1, 2, 20, 21, and 22 respectively. Claims 17-18 and 29-31 recite the methods of the parent

claims, "further comprising immobilizing the fusion protein". The claims do not clarify when the fusion protein is immobilized in relation to the steps recited in the parent claims, in other words is the fusion protein immobilized before it is bound to the second member of the binding pair, after it has bound the second member of the binding pair but before it binds to the target binding molecule, or after it has bound both the second binding pair member and the target binding molecule. As such, the metes and bounds of the claim cannot be determined.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, the technology center fax number is (703) 872-9306. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER